REMARKS

The Present Invention

The present invention is directed to a combination of specified retinoids and specified retinoid boosters that are stabilized in a composition, wherein each constituent of the oil phase of the oil-in water emulsion has a peroxide value (POV) of less than or equal to about 12, preferably less than or equal to about 6. Controlling the POV is particularly important with combination of retinoids and boosters, to ensure a retinoid half-life of at least 20 days at 50 deg. C.

The present invention provides the dual benefit of enhancing retinoid efficacy within the skin while increasing the *stability of the retinoids in the composition* by the removal of any starting materials having a POV of greater than 12, and preferably greater than 6. See Specification at page 32.

The POV specification is critical for removing oil impurities that would have POV of greater than 12 and would thereby contribute to retinoid instability. For example, while the general category of mineral oil is known, depending on the commercial source of the oil, it may have undesirable impurities with POV greater than 12. Specifying the POV in the present claims excludes these impurities, or removes oils with POV greater than 12, which would promote instability. The resulting inventive compositions extend retinoid stability. Support for "removal of any starting materials having a peroxide value of greater than 12 and preferably greater than 6 may be found on page 32 and elsewhere in the Specification.

Claims 1-2, 7-8, 13 and 15 Are Not Obvious Under 35 USC § 103

Claims 1-2, 7-8, 13 and 15 were rejected under 35 U.S.C. 103(a) as being unpatentable over Granger et al. (USPN 5,716,627) in view of Potter et al. (US 5,620,692). *Applicants respectfully traverse.*

Claims 1 and 7 specify that the inventive compositions are to ensure a retinoid half-life of at least about 20 days at 50 deg. C. *The Examiner's position notwithstanding, this limitation is directed to a selection of oils that will lead to stability of retinoids in the presence of boosters at elevated temperature. Such a selection is not suggested in the cited references.*

Granger *'627* teach a skin-conditioning composition comprising *a synergistic combination of* (a) retinol or retinyl ester, (b) azole (e.g. climbazole), (c) LMEA, and (d) cosmetically acceptable vehicle. The Office Action admits that *Granger '627 does not teach that each ingredient in the oil phase should have POV as recited* in the claims, i.e. that each constituent of the oil phase of the oil-in water emulsion has a peroxide value of less than or equal to about 12, preferably less than or equal to about 6. As Granger *'627* fail to disclose or suggest a POV, Potter et al. are cited. However, Applicants respectfully submit that Potter et al. fail to remedy the deficiencies of Granger '627. As such, a *prima facie* case of obviousness has not been made out.

Potter et al. fail to remedy the deficiencies of Granger '627 for the following reasons. While Potter et al. may define the POV parameter in general, it fails to teach or suggest specific materials (*e.g. retinoids)* and/or specific POV values as presently claimed. Potter et al. relate to a process to prepare oat oil compositions. See Abstract. The antioxidants in oat oil are esters of caffeic and ferulic acid, see Col. 1, lines 45-51,

which have nothing to do with the oils claimed in the present invention and are antioxidants for skin lipids, while the low POV oils claimed herein have a stabilizing effect on other components of the cosmetic composition. *While Potter et al. may exemplify an oat oil with POV of zero, they fail to suggest a workable range to less than 12, i.e., a range demonstrated to be workable at elevated temperatures for stability of retinoids according to the present invention.*

There Is No Inherency

The Examiner's position at pp. 3 and 7 notwithstanding, the prior art composition does not comprise "the same consitutuent of the oil phase of the emulsion." The perfume in the Examples is not specified and therefore it does not specify all oil components with a POV of less than or equal to 12. Applicants respectfully submit that not all the named ingredients in the cited references are the same, and they will not "invariably" possess the same characteristics. For example, while the general category of mineral oil is known, depending on the commercial source of the oil, it may have undesirable impurities with POV greater than 12. Specifying the POV in the present claims excludes these impurities, or removes oils with POV greater than 12, which would promote instability. The resulting inventive compositions extend *retinoid stability, defined by the concentration of retinoids in their original chemical form after a defined storage duration and temperature*. See present Specification at page 32.

There is no disclosure of *retinoid stability for extended time at an elevated temperature*. The mere fact that the cited art could be modified as proposed in the Office Action is not sufficient to establish a *prima facie* case of obviousness. See In re Fritch, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992). The Office Action must explain why the cited art would have suggested to one of ordinary skill in the art the desirability of the modification. See Fritch, 23 USPQ2d at 1783-4. The Office Action has not

provided such an explanation. For these reasons, it is concluded that the Office Action has not carried the burden of extablishing a *prima facie* case of obviousness of the invention recited in any of the Applicants' claims.

Objective Evidence Presented in Declaration Must Be Considered

A focus of the present invention is retinoid stability, rather than the stability of the oils themselves in the oil phase of the emulsions. The Declaration by Dr. Iobst *provides* objective evidence of stability of the *retinoids in the* inventive compositions as claimed. The data show that controlling the POV of the oil phase at below about 12 achieves a *retinoid* half-life of at least about 20 days at 50 deg. C, *i.e, an extended period of time at elevated temperature. This is objective evidence. Furthermore, Dr. Iobst states, based on the data, that these results of thus stabilizing retinoids are unexpected to her as one skilled on the art.*

Claims 14 and 16, *Requiring a Combination of LAMEA and PAMEA, AMFA and alpha-Ionone*, Are Free of the Art

Claim 14 *and 16 were* rejected under 35 U.S.C. 103(a) as being unpatentable over Granger et al. (USPN 5,716,627) and Potter et al. as applied to 1-2, 7-8, 13 and 15, and further in view of Granger et al. (WO 98/13020) (to remedy lack of disclosure of alpha-ionone in the primary references).

Claim 14 requires the presence of the booster alpha-ionone (B1 booster) in combination with the booster LAMEA, which in combination with the retinoid and the selected oils at POV of less than or equal to about 12, are free of art.

Claim 16 requires the booster alpha-ionone (B1) in combination with the booster(s) AMEA or PAMEA (fatty acid amide, B1 booste.s), which in combination with the retinoid and the selected oils at POV of less than or equal to about 12.

Granger '627 and Potter have been distinguished above. Furthermore, Potter is directed to stability of the oat oil itself, having POV of 0-50 at unstated temperature, presumably room temperature. Importantly, the present invention relates to stability of retinoid which is combined with an oil having POV less than 12 and booster (which has destabilizing effect) at elevated temperature. According to the present invention, stability of retinoid is tested and expressed at elevated temperature as an accelerated measure of long term stability. Potter do not disclose or suggest stabilizing retinoid in the presence of boosters (including alpha-ionone) to a level of at least 20 days at an elevated temperature of 50 deg. C as presently claimed.

The combination with Granger '020 is improper an in any event does not lead to the present invention. Granger et al. (WO 98/13020) teaches away from using a fatty acid amide. *Evidence of teaching away is in the reference itself. Granger '020 in the Summary, on page 3 and in Claim 1 on pp. 52 and 54, state: "compound is not a fatty acid amide ...".* Therefore, a retinoid composition comprising LAMEA (B1 booster, fatty acid amide) would not be within the scope of Granger WO'020, and it would not be proper to combine it with Granger '627 *and Potter. The Office Action p. 7 position to the effect that Granger'020 "does not provide any teaching or suggestion that the retinoid boosters of the '020 reference should not be combined with fatty acid amides" notwithstanding, there is no suggestion or motivation for one skilled in the art to combine the primary references with Granger'020. Granger'020 fails to provide a suggestion or motivation to combine retinoids with fatty acid amides.* Accordingly, Claims 14 and 16 are in condition for allowance.

An obviousness rejection is proper only when "the subject matter as a whole would have been obvious at the time the invention was made ..." (emphasis added). 35 U.S.C. 103. Applicants respectfully submit that the Office Action has improperly chosen certain aspects of one reference and combined them with aspects of other references, without showing where the motivation is to combine them to come up with the subject matter of the present invention as a whole, within the meaning of 35 U.S.C. 103. *Furthermore, the Office Action has improperly selected some portions of Granger '020 while discounting other portions of Granger '020 that specifically specify the absence of fatty acid amides.* Applicants submit that the pending claims are not obvious over the cited references, under 35 U.S.C. 103, especially in view of the present Amendment. Reconsideration and withdrawal of the rejection is respectfully requested.

Claims 14 and 16 are believed to be in condition for allowance.

Conclusion

The Granger et al. references *and Potter et al.,* either alone or in combination, do not address the problem to which the present invention is addressed, i.e., improvements in stability of retinoids *at elevated temperatures, in the presence of destabilizing boosters,* achieved by controlling POV of each constituent of the oil phase of the oil-in-water emulsion, while increasing the effectiveness of the retinoids.

Those skilled in the art would not have identified among the various materials a special stabilizing effect of oils with POV of less than about 12 when used in a formulation with retinoids and retinoid boosters from a mere reading of the cited art.

In view of the foregoing amendments and comments, Applicants request the Examiner to reconsider the rejections and now allow the claims.

If a telephone conversation would be of assistance, Applicant's undersigned attorney invites the Examiner to telephone at the number provided.

Respectfully submitted,

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